Amendment One (1)

OFFICE OF ACQUISITIONS
National Institute of Allergy & Infectious Diseases ("NIAID")
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Rockville, Maryland 20852

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Purpose of Solicitation Amendment 1:

The purpose of Amendment 1 is to revise the deadline for receipt of proposals, respond to questions received regarding this solicitation, and to provide a final date for the submission of questions. Any questions that have been submitted but not yet addressed will be answered in the next amendment.

Deadline for Receipt of Proposals: September 15, 2015, 5:00 pm Eastern **(CHANGED)**

> **Offerors must acknowledge receipt of this Amendment (as well as other amendments) on their proposals.** Failure to receive your acknowledgement of this Amendment may result in rejection of your proposal. Except as provided herein, all terms and conditions of the solicitation remain unchanged and in full force and effect.

This solicitation is amended as set forth below.

A. Final date to submit questions regarding this solicitation:

The last day to submit questions regarding this solicitation is **August 28, 2015.**

B. Below is the Government's response to questions received regarding this solicitation:

Technical Questions:

1. The Presolicitation Notice indicates that broad spectrum anti-bacterial and antivirals should have activity against one of the listed organisms and one other NIAID Category A, B, or C agent.

    a. **QUESTION:** Will a proposal be considered if it proposes two of the listed organisms, e.g., Bacillus anthracis and Francisella tularensis, or is another organism required?

    ANSWER: Proposals may include two of the listed biodefense organisms (e.g. *Bacillus anthracis* and *Francisella tularensis*). Please refer to Section II. B., Technical Objectives, of the BAA, which states "Only agents identified as NIAID Category A, B and C Priority Pathogens are eligible as proposed candidates/products for this solicitation."

    This section of the BAA also states, in part, "Therapeutics targeted under this BAA are specified as the following: Broad spectrum anti-bacterial: Therapeutic with activity against one of the following bacterial pathogens: Bacillus anthracis, Francisella tularensis, Yersinia pestis, Burkholderia pseudomallei, B. 5 mallei AND in addition, activity against one other NIAID Category A, B or C bacterial threat agent.

    b. **QUESTION:** If I have an interest in Salmonella, does the animal model require oral administration of Salmonella to be responsive?

    ANSWER: While there is no requirement for specific animal models to be used, animal models must show evidence of relevant therapeutic activity.

    c. **QUESTION:** Category C includes antimicrobial research including engineered threats and naturally occurring drug-resistant pathogens. Will carbapenem resistant *Klebsiella pneumonia* be considered?

    ANSWER: Yes.

    d. **QUESTION:** Below Category C is a list entitled Additional Emerging Infectious Diseases/Pathogens, which includes *Clostridium difficile*. Will *C. difficile be considered?*

    ANSWER: Yes.

2. **QUESTION:** The solicitation states that the development of licensed products as new formulations or for additional clinical indications are not the target of this BAA (section II.B, last paragraph). Does NIAID define licensed as synonymous with FDA-approved and if so, please confirm whether a product approved in Korea but not in the US would be eligible for consideration under this BAA?

   ANSWER: Development of any licensed products, including products licensed in countries other the US, is NOT eligible for funding under this BAA.

3. **QUESTION*:*** The solicitation states that NIAID estimates that two to five contracts may be issued for a total cost (direct and indirect costs combined) of up to $15.3 million in Fiscal Year 2016 for all awards. Acknowledging that the total cost for the award(s) may vary depending upon the scope of the project and the technical objectives of the award(s), does that include all options? Additionally, is each awarded contract anticipated to have a total cost of $15.3 million or the total cost of all awarded contracts?

   ANSWER: The anticipated FY16 funding is total of $15.3 million for the Base Period only (not including options) for all awarded contracts (not each contract).

4. **QUESTION:** Development of serum-derived products is excluded. Does this also apply to monoclonal antibodies?

   ANSWER: Development of monoclonal antibody products is included under this BAA.

5. **QUESTION:** The BAA defines a qualifying therapeutic candidate several ways, some of which appear to require direct anti-bacterial/anti-viral/anti-toxin activity and some of which appear to include therapeutics that can mitigate the effects of these infections. Would molecules that address toxic host immune reactions, such as cytokine storm, in reaction to Category A, B, or C infections be appropriate to submit to this BAA solicitation?

   ANSWER: Yes, but any candidate must be efficacious in a therapeutic animal model of a targeted disease.

6. **QUESTION:** The BAA states a requirement for the proposed therapeutic to be broad spectrum and small molecule in nature. The section addressing the anti-toxin work seems to drop this broad spectrum requirement and I was writing to find out if my interpretation is correct. Is there active interest in a combined antibody based therapy for two of the three components of the anthrax toxin?

   ANSWER: Yes, monoclonal antibodies against toxins will be considered.

7. **QUESTION:** Do you consider applications that do not include clinical studies in the application to be responsive to the BAA? Or are you expecting to see clinical studies in the application?

   ANSWER: Clinical studies are required to be part of the proposal and appropriate to the stage of product development. Pivotal efficacy studies such as Phase 3 clinical trials and pivotal studies to the meet the regulatory requirements for licensure under the "Animal Rule" will not be supported.

8. **QUESTION:** Will a plan for adjunctive therapy be considered, or are you expecting the products studied to be stand-alone agents that directly kill bacteria?

   ANSWER: Development of the host-targeting adjunctive therapy will be considered. The drug must work in a therapeutic model of disease, meaning that the candidate must clearly demonstrate efficacy when administered after signs or symptoms of disease are present. If the therapy is not efficacious as a stand-alone product, a companion agent must be clearly identified.

9. **QUESTION:** Would the following program fit within the BAA scope? A Phase 2 clinical trial for an antiviral compound that already has Phase 1 data and meets the criteria of a broad spectrum antiviral as defined in the BAA. The program would include activities related to performance of Phase 2 clinical trials.

   ANSWER: While the primary intent of the BAA is to support development of new therapies through Phase 1 clinical development, all proposals must include a clinical development plan that is appropriate to the stage of product development. Pivotal efficacy studies such as Phase 3 clinical trials and pivotal studies to meet the regulatory requirements for licensure under the "Animal Rule" will not be supported.

10. **QUESTION:** Will the targeting of host factors with the goal to mitigate disease caused by Ebola and Marburg virus be considered or does the drug has to have the direct antiviral effect? Will a proposal be considered if the aim is to mitigate disease development caused by influenza A viruses and Ebola/Marburg without directly targeting the virus?

    ANSWER: Yes. The drug must work in a therapeutic model of disease, meaning that it must show efficacy when administered after signs or symptoms of disease are present.

11. **QUESTION:** My question is in regard to the statement about activity against discrete strains, species or serotypes within a virus genus. So for example for Ebola virus there are 5 distinct species (Zaire, Sudan, Bundibugyo, Ivory Coast, Reston) where vaccines or drugs against one do not usually provide protection against another. Same thing for Marburg virus where there are two genetically distinct lineages where for example a vaccine or drug against the Angola strain may not protect against the Ravn strain. Would a drug that protected against say more than species of Ebola or against both of the genetically distinct strains of Marburg qualify under this BAA?

    ANSWER: In general, discrete viruses are being regarded as different if immunity to one virus/strain would not confer immunity to another strain. As an example, there are numerous influenza virus strains that meet this classification. Since it is unknown whether the genetic difference for Marburg strains in question would similarly not confer immunity, the interpretation for the purposes of this BAA would be to consider genetic strains of Marburg virus to be different and therefore, would meet the criteria for activity against two or more strains of viral pathogen. Therapies that provide benefit against, in this instance, all Filoviridae members, are of particular interest compared to therapies that only act on a limited number of virus family members.

12. **QUESTION:** The BAA requires that a therapeutic candidate must be "An agent with demonstrated *in vivo* activity in an appropriate therapeutic model of disease". Would a therapeutic candidate that has demonstrated *in vivo* activity against *Neisseria meningitidis*, which also binds to *Yersinia enterocolitica* and *Francisella tularensis* (but has not yet been tested in animal models against these two pathogens), potentially qualify as a broad spectrum therapeutic candidate?

    ANSWER: Yes. In vitro evidence may be enough if the mechanism of action is presumed or known to be the same for *Neisseria* and biodefense pathogens.

13. **QUESTION:** The solicitation indicates that the single agent meets the following 3 criteria:
    a. A drug or a biological product intended for use in the cure, mitigation, or treatment of two or more bacterial or viral pathogens; and
    b. An agent with demonstrated in vivo activity in an appropriate therapeutic model of disease; and
    c. An agent that will complete evaluation in a Phase 1 clinical trial within the 5-year proposed period of performance.

    For our project we have an entity which shows in vitro antiviral activity against 3 of the named pathogenic viruses. Also, we have not as yet assessed the activity in animal models of the other pathogenic viruses. Is this necessary for the application?

    ANSWER: The drug must work in a therapeutic model of disease, meaning that there must be evidence of in vivo efficacy.

14. **QUESTION:** We have demonstrated antiviral activity in vivo in an animal model of IFV when administered after viral infection and are currently generating the data set for effect on clinical signs associated with IFV infection. We expect this to be completed late August/early September. We may therefore not have the complete in vivo data set by the submission deadline. Are we required to have a full data set for the in vivo activity in all target viruses in order to submit a proposal for this BAA?

    ANSWER: You may already have the needed data based on your statement: "For action 2, we have demonstrated antiviral activity in vivo in an animal model of IFV when administered after viral infection."

15. **QUESTION:** As our understanding that antiserum or Hyperimmunes might not be eligible under this BAA, we would like to confirm whether blood plasma derived biologic molecules such as inhibitor proteins are eligible.

    ANSWER: Blood plasma derived biologic molecules such as inhibitor proteins are ineligible. Blood-derived products are not supported by this BAA.

16. **QUESTION:** Our product is based on an approved drug for which the patent has already expired (not a licensed product). Does it make it suitable for this BAA application?

    ANSWER: Contracts awarded under this BAA will not target development of licensed products as new formulations or for additional clinical indications, including products

reformulated for a different route of administration. Since approved (for marketing) is the same as licensed, this drug is not suitable for this BAA solicitation.

17. **QUESTION:** Offerors are to provide a Protocol Synopsis for each proposed clinical trial…" Will the standard NIH template for protocol synopses satisfy this requirement?

    ANSWER: Yes

18. **QUESTION:** Will this BAA support the development of product candidates through advanced clinical development (e.g., Phase 2 and Phase 3)?

    ANSWER: The primary intent of the BAA is to support development of new therapies through Phase 1 clinical development. Proposals should include a clinical development plan that is appropriate to the stage of product development. Pivotal efficacy studies such as Phase 3 clinical trials and pivotal studies to meet the regulatory requirements for licensure under the "Animal Rule" will not be supported.

Business Questions:

1. **QUESTION:** Regarding "Information and Physical Access Security", can you explain under what circumstances applicants will have "routine (1) physical access to an HHS-controlled facility; (2) physical access to an HHS-controlled information system; (3) access to sensitive HHS data or information, whether in an HHS-controlled information system or in hard copy"? I don't anticipate having access to such a facility or to sensitive HHS data or information. Is the contract itself considered "sensitive HHS data or information"?

   ANSWER: This language is included in the solicitation and based upon the work anticipated to be performed. For proposal purposes, use the levels identified in the solicitation.

2. **QUESTION:** Can the CVs for key personnel be included as an appendix to the Scientific and Technical Approaches volume and therefore be outside the page limitation for that volume?

   ANSWER:
   No. As stated in Section VI, Technical Proposal Instructions, of the BAA, The Technical Proposal should include all information relevant to documentation of individual training, education, experience, qualifications, and expertise of proposed personnel, as well as availability necessary for the successful completion of all contract requirements. Clearly identify who is proposed as Key Personnel. Limit CVs to 2-3 pages, provide selected references for publications relevant to the scope of this BAA, and include experience with projects of similar scope, size and complexity carried out by the Offeror and any proposed subcontractors over the past 5 years.

3. **QUESTION:** The BAA notes that offerors are to "submit an E-Authentication Risk Assessment, E-Authentication Threshold Analysis and a System Security Plan with their Final Proposal Revision…" Can the government confirm whether the requirement applies to a future submission and not the submission due on August 31, 2015?

ANSWER: Correct. That requirement is referring to a future submission.

4. **QUESTION**: We are unable to access the link for the "Breakdown of Proposed Estimated Costs (plus fee) with Excel Spreadsheet" on page 7 (Section 2.b).

   ANSWER: Functionality of the link in the solicitation has been confirmed. The Excel spreadsheet will be included as an attachment to this Amendment and the website is also provided below:
   http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/spshexcl_dec2012.xlsx

5. **QUESTION:** We are unable to access the link for the Technical Proposal Cost Summary on page 24 (Section 4.b.15).

   ANSWER: Functionality of the link in the solicitation has been confirmed. The document will be included as an attachment to this Amendment and the website is also provided below:
   http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/Tech-Prop-Cost-Summ.pdf

6. **QUESTION:** We are unable to access the link for the Labs & Scientific Resources on page 24 (Section C.1, page 24).

   ANSWER: Functionality of the link in the solicitation has been confirmed. The website is provided below:
   http://www.niaid.nih.gov/LabsAndResources/resources/DMIDClinRsrch/Pages/default.aspx

7. **QUESTION:** Is the base effort expected to be one year in duration?

   ANSWER: The base effort is not limited to one year in duration. The duration depends on the individual projects and definitive milestones. Furthermore, options may be performed concurrent with base period activities. The exercise of options are triggered by meeting criteria that are defined in the Statement of Work.

8. **QUESTION:** Will the Government consider extending the proposal submission deadline?

   ANSWER: Yes, the revised proposal submission deadline is September 15, 2015 at 5:00 p.m. EDT.